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Developments in Neuropsychological and Neurophysiological Assessment

An Overview of Progress and Products of the JWGD3 Level I Neuropsychology Task Area Group

Dennis. L. Reeves (1)
Steven. L. Taube (2)

1. **Naval Medical Research Institute, Bethesda, MD**
2. **Walter Reed Army Institute of Research, Washington, D.C.**

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Level I Task Area Group (TAG)

WRAIR AAMRL NMRI NIDA/ARC
USARIEM NAMRL
USAARL

Disciplinary Expertise:

Neurospychology Neuropsychiatry
Neurophysiology

Mission

To develop an automated Clinical Neuropsychological/Neurophysiological Assessment Battery/System

Purpose

To provide a standardized and clinically relevant "quick but comprehensive" assessment of nervous system integrity for screening Chem Def biomedical drugs.

Products

1. Neuropsychological Test System (NPTS)
2. Neurophysiological (Evoked Potential) Assessment Battery/System (NP-PAB)
3. Psychomotor/Neuromuscular-tone tests and instrumentation

The Level I Screen

The Level I Screen represents the first of three major and interdependent assessment levels in the Tri-Service JWGD3 MIL PERF treatment/pretreatment drug screening program. The primary objective of this "first look" at drug effects on human performance is to identify neurological systems and functions that indicate adverse effects from drug administration. This information will in turn provide direction for the Level II Residential Screen, and will yield instrumentation and testing protocols for Level III (i.e., drug and stress) and Level IV (i.e., field-test) studies.

Some of the drugs that enter the chemical defense program have a long history of medical use, e.g., atropine and pyridostigmine. There exists a body of clinical and research information about these drugs suitable to the design and support of Level II and Level III screening efforts. As new drugs are developed, such information may be inappropriate, incomplete, or absent. The latter situation will arise most often in the case of new drugs that lack an extensive history of use. To obtain the necessary data expeditiously, the Level I Task Area Group (TAG) has placed emphasis on development of an automated, standardized, and clinically relevant assessment of nervous system integrity. The character of this phase of the Level I Screen is designed to meet the requirements of the U.S.Food and Drug Administration's Phase I drug development process. In a further phase of the JWGD3 MIL PERF screening program, the Level I batteries will provide for rapid, mass screening in field settings. Several features of the Level I batteries make this possible. For example, cognitive testing can be accomplished on multiple subjects concurrently using tasks that require no preliminary training. In addition, individual results can be evaluated on site and available immediately. Finally, the data obtained is collected digital form and can be easily transmitted to a central mainframe computer for further analysis to elucidate inter-subject patterns of response.

The Level I Screen will include two major subsets (an automated neuropsychological and an neurophysiololgical "evoked-brainwave-potential" assessment battery/system), and a minor subset of selected psychomotor/neuromuscular tests. This third group has been developed to meet an immediate need for assessment of carbamate myopathy associated with administration of pyridostigmine bromide.

Progress and products associated with development of these subsets constitute the central focus of this report, and are described on an individual basis in the following sections.

Subset 1

Neuropsychological Test System (NPTS) and Evaluation

The JWGD3 MIL PERF Chemical Defense Performance Assessment Plan (3 nov 1983) defined a requirement for Level I rapid screening of subjects to assess neuropsychological status both pre- and post-prophylactic treatment. This type of assessment would involve the comprehensive evaluation of brain behavior relationships and yield information related to the level of impairment, likelihood of focal or generalized brain dysfunction, and a description of the status of cognitive, perceptual, and motor functions. Conventional neuropsychological assessment procedures that employ batteries requiring six to eight hours of individualized testing time are unsuitable for the rapid screening and repeated measures requirements of the JWGD3 MIL PERF program.

The task of rapid assessment in a drug treatment paradigm, is most effectively accomplished through employment of computer-based automated neuropsychological testing in a screening or adaptive mode. Hence, the JWGD3 MIL PERF/Level I TAG is sponsoring development of an advanced automated Neuropsychological Test System (NPTS), that will employ the latest developments in computer technology and biomedical research in psychology.

A primary objective of this effort is to sponsor and direct the design, development, construction, and validation of a fully-automated neuropsychological test system capable of running on a micro-computer based system. Required characteristics for the NPTS are as follows:

Suitability for mass screening in laboratory and field settings;

Capability to test a comprehensive range of neuropsychological functions that include sensory, perceptual, and cognitive abilities and their reactions to neurochemical stressors;

Sensitivity to detect interactive and independent effects of chemical agents, and other stressors such as heat, cold, hunger, thirst, and fatigue;

Capability to utilize repeated-measures testing procedures to assess changes in level of performance between pre and post-treatment conditions;

The capability to sample neuroanatomic locations and neurochemical systems to the extent that functions can be localized;

The capability to test in one of three modes, screening, adaptive, and in-depth;

The flexibility to provide the operator with multiple options for ordering subtests, presenting test data, and computer-assisted interpretation of results.

This project is primarily under the supervision of LTC Steven S. Taube, Department of Behavioral Biology, Walter Reed Army Institute of Research (WRAIR). Final contractual negotiations are currently underway with the signing of a contract anticipated in April 1986.

Subset 2

Neurophysiological Performance Assessment Battery

(NP-PAB)

Early on, it was recognized that the Level I TAG possessed an established and skilled neurophysiological subdivision as well as sophisticated neurodiagnostic evoked potential recording systems. As a result a decision was made to capitalize on and enhance this in-house resource by developing a standardized Tri-service neurophysiological performance assessment battery (NP-PAB). Included in this effort is a "networked" operating system and central archive for JWGD3 MIL PERF related data. The NP-PAB will serve two important functions for the chemical defense program: one will be as an independent Level I neurotoxicological screen while the NPTS is being developed; and the other is as a complementary Level I/II metric that will allow concurrent neurophysiological and cognitive performance assessment. The latter function will augment Level II UTC-PAB performance data by simultanesouly providing relevant neurodiagnostic information.

During the past two decades, a sophisticated methodology and theoretical framework has evolved from research on various measures of sensorily evoked and cognitively "invoked" electrophysiological responses. As a result, signal averaging has emerged as an established neurodiagnostic tool, and evoked potentials (EPs)have proven to be a reliable means to determine the functional integrity of the central and peripheral nervous system. Pattern-reversal visual (PREPs), steady-state EPs, brainstem auditory (BAER), and short-latency somatosensory evoked potentials (SEPs), are among the best established indices of function in their respective sensory systems. In addition, they have been shown to be sensitive indicators of neurotoxicity. These four tests form the core sensory-EP evaluation which is designed for rapid assessment of cortical, brainstem, and peripheral nervous system integrity. Cognitive functions may be assessed by eliciting the P300 event-related potential (ERP) in a variety of paradigms.

The Level I TAG has established a set of nine EP tests and has standardized the protocols to form the basis of a "Mark I" NP-PAB Library. These are listed as follows:

1. Steady-State Evoked Potential
2. Pattern Reversal Evoked Potential (PREP)
3. Brainstem-Auditory Evoked Response (BAER)
4. Somatosensory Evoked Potential (SEP)
5. Event-Related P300 (oddball-auditory ERP)
6. Continuous Performance Task (ERP)
7. Sternberg Memory Task (ERP)
8. Selective Attention (ERP)
9. Frequency Analysis of the EEG

Currently under evaluation as a candidate for item 10 is Topographical Mapping of Evoked-Electrocortical Brain Activity (also known as Brain Electrical Activity Mapping (BEAM)).

The operating system is based on the interfacing of two major electrodiagnostic units. The Nicholet Pathfinder II and AAMRL's Neuropsychological Workload Test Battery (NWTB) system. These two systems are complementary, in that the Pathfinder II has been primarily developed for diagnosis of sensory system defects, and the NWTB has emphasized assessment of Event-Related "cognitive" Potentials (ERP). In addition, the NWTB system incorporates the option to measure heartrate, eyeblink (as a measure of stress and workload) and EMG concurrently with evoked-potential measures.

The third sub-unit of the NP-PAB operating system is the Data Storage System (located at NMRI) which will serve initially as a central archive for evoked potential data and act as the hub for a JWGD3 NP-PAB network.

Subset 3

Selected Psychomotor/Neuromuscular-tone Tests

This minor subset of the Level I screen consists of a limited, (basic-abilities), set of tests designed for detecting breakdown at the neuromuscular junction. These tests include the following:

1. Automated Intentional/Micro-Tremor Device
2. Tapping Test
3. Grip Strength
4. Zero-Order Zita-Tracking Task

As stated in the introduction, these tests were assembled to address immediate needs for a Level I neuromuscular-tone assessment for pyridostigmine studies. No further in-house development of a Level I psychomotor assessment battery is planned. However, it should be noted that this limited effort has produced some very good and sensitive neurodiagnostic instruments which we do plan to use in future JWGD3 MIL PERF sponsored studies.

Current Status and Future Plans

NPTS: An extramural support contract will be let in April FY86. Primary supervision will be from WRAIR with support from NAMRL.

Interagency collaboration with the Veterans Administration is being planned for development of a sophistocated expert system for data interpretation and for acquisition of data for validation and standardization.

NP-PAB: The core battery has been defined and standardized protocols have been established. An operating system, and data archive has been assembled from off-the-shelf and prior developmental efforts.

Future plans are to establish a common data base and laboratory norms among participating labs. NMRI will serve as the central archive. AAMRL and NAMRL have been designated as product improvement labs and will sponsor evaluation and development of Level I/II NP-PAB tests (including BEAM). USARIEM, USAARL, and NMRI, will conduct LEVEL I/III (i.e., evoked-potential and environmental stress/ simulator studies). It is anticipated that all major components of the network will be in place by the beginning of FY88 and a normative data pool will be established shortly thereafter.

Psychomotor/Neuromuscular-tone tests: Tests will be in place and ready for testing by the end of FY86.

Proposed Level I TAG Laboratory Assignment

Subset 1
Neuropsychological Assessment Test System (NPTS) Labs

1. WRAIR
2. NAMRL

Subset 2
Neurophysiological Performance Assessment Battery (NP-PAB) Labs

NP-PAB Development Facilities
1. NAMRL
2. AAMRL
3. NIDA/ARC ("Beta" testing)

Data-Base Archive
1. NMRI

Level I/III NP-PAB LABs

1. NMRI (NP-PAB + Thermal Extremes)
2. USARIEM (NP-PAB + Thermal Extremes)
3. USAARL (NP-PAB + Helocopter Simulator)

DISCUSSION AND COMMENTS

Neuropsychological test System Report LTC Steven Taube, MC

Comment: Dr. Hegge

Early in the program great emphasis was placed on the requirement to address the needs of the operational community. I think there is also a requirement to speak to the needs of the clinical community. We must have, at the start of our process, a set of evaluation tools that are conservative and acceptable clinical assessment instruments that will be familiar to organizations like the Food and Drug Administration. There is no reason to believe that communications about the arcana of performance evaluation will be easier with one community than with the other. Also, a test system that is capable of handling people with a minimum amount of pre-training and a minimum specification of prior behavioral repetiores will be extremely useful in field trials stage. The Neuropsychological Test System will have the capacity to characterize field populations with a fair degree of facility.